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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,397	09/26/2003	Ronald Rooke	032751-094	2721

21839 7590 10/15/2004

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EXAMINER	
CHEN, STACY BROWN	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/670,397	ROOKE, RONALD	
	Examiner	Art Unit	
	Stacy B Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *1-21,26 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-25 and 27-33* is/are rejected.

7)☒ Claim(s) *25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/969,770.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/26/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group III, claims 22-25 and 27-33 in the reply filed on July 30, 2004 is acknowledged. The traversal is on the following grounds:

- Applicant submits that the inventions of Groups III and I, and II and IV are closely related, and that a proper search of any one group would necessarily constitute a proper search of the other groups.
    - This is not found persuasive because a search for any one Group is not co-extensive for any other group. Searching the prior art for an adenoviral vector containing the E3 proteins 14.5K and 10.4K, will not necessarily reveal the instantly claimed methods of using an adenoviral vector containing the E3 proteins of 14.7K, 14.5K and 10.4K. A comprehensive search for Groups II and I, and II and IV constitutes a serious burden on the Office.
- Applicant submits that the restriction requirement places an unnecessary burden on both the Applicant and the USPTO. The filing of multiple applications that contain the same disclosure and require the same search is an example of how the restriction requirement is burdensome to the Applicant and the Office. Applicant submits that withdrawal of the restriction is in the best interests of the economy, the USPTO, the public-at-large and Applicant.
    - This is not found persuasive because the restriction of a patent application to one invention is in the best interests of both Applicant and the Office. The search and examination of multiple inventions in a single application imposes a serious

search burden on the Office in certain situations, such as the instant application. Further, under certain conditions, Applicant is entitled to rejoinder of method claims involving an allowable product claim. (See the Restriction Requirement of July 13, 2004, pages 3 and 4, outlining the rejoinder process.) Rejoinder of the method claims of the instant invention, if they are related to an allowable product claim by containing all of the limitations of the allowable product claim, would afford Applicant the opportunity to prosecute multiple inventions in the instant application. (Note that not all of the instant method claims contain all the limitations of the elected product.)

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-34 are pending. Claims 22-25 and 27-33 are under examination. Claims 1-21, 26 and 34 are withdrawn from consideration, being drawn to non-elected inventions.

Specification

3. The disclosure is objected to because of the following informalities: The status of all parent applications in the specification (first page, first line) must be updated. Appropriate correction is required.

Claim Objections

4. Claim 25 is objected to because of the following informality: In claim 25, cytomegalovirus is misspelled as "cytomergalovirus". Appropriate correction is required.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 22, 25 and 27-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Bout *et al.* (EP 0707071 A1, herein, "Bout"). Claim 22 is drawn to a recombinant adenoviral vector in which at least part of the E3 (E=early) region is deleted or is rendered non-functional. The retained E3 sequences encode a functional 14.5K protein and a functional 10.4K protein. The 14.5K protein and 10.4K protein are also called RIDα and RIDβ (Receptor Internalization and Degradation), respectively. A functional 14.5K protein and a functional 10.4K protein associate to form a complex (RID complex). The recombinant viral vector contains a gene of interest, which can be homologous or heterologous to the host cell into which it is introduced (specification, col. 10, lines 22-24). The retained E3 sequences and gene of interest are operably linked to regulatory elements allowing their expression in a host cell. The retained E3 sequences that encode a functional 14.5K and 10.4K protein are located in the adenoviral vector at a location where the E3 region normally resides and in sense orientation (the naturally-occurring orientation) relative to the direction of transcription of the native E3 region. The specification discloses that since the retained E3 sequences are located where the E3 region normally resides, the retained E3 sequences can be those that naturally occur in said vector (specification, col. 8, lines 36-44). Claim 22 broadly encompasses a recombinant adenoviral vector that has had a portion of the E3 region deleted or rendered non-functional, yet retains naturally-occurring E3

sequences that encode a functional 14.5K and 10.4K protein. The retained E3 sequences are placed under the control of the immediate early promoter of the cytomegalovirus (CMV promoter). Also claimed is a viral particle, isolated host cell and composition (with a carrier) comprising the vector of claim 22. Specifically, the viral particle comprising the adenoviral vector of claim 22 has its E1 region deleted-in-part or rendered non-functional.

Bout discloses recombinant adenoviral vectors that have a deleted/non-functional E1 region and at least a functional part of the E3 region (Bout, page 3, lines 32-33). Bout teaches that some cell types (mouse liver cells, baboon lung cells and cotton rat lungs, for example) are capable of supporting limited synthesis of adenoviral proteins in E1 deleted adenoviruses (Bout, page 3, lines 32-57). Bout discloses the use of these cell types for hosting E1-deleted adenoviral vectors that retain some E3 functional protein in order to reduce host cell responses against infected cells. In particular, Bout teaches that the E3 14.7 K protein and the RID complex are useful for reducing host cell responses against infected cells (page 3, lines 1-29). Bout discloses that it is not necessary to retain the entire E3 region, only the proteins that contribute to reducing host cell responses against infected cells. Bout does not explicitly disclose the position or orientation of the sequences that encode the retained E3 proteins, however, the deletion of some portions of the E3 region would leave the desired portions in their original position (where E3 naturally occurs) and in the sense orientation (how the sequences naturally occur). It is the Office's position that the position/orientation of the retained E3 sequences of Bout's adenoviral vector is an inherent property of the vector described (Bout, page 4, lines30-31). The adenoviral vector also may contain a gene of interest that is expressed in the host cell (Bout, page 4, lines 38-41). The CMV promoter may be used with the adenoviral vector (Bout, page 4, lines 49-52).

The adenoviral vector/host cell is in a pharmaceutical formulation with suitable means for administration (Bout, page 21, claim 16). Therefore, the claims are anticipated by Bout.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bout as applied to claim 22 above, and further in view of Krajcsi *et al.* (*Journal of Virology*, August 1996, 70(6):4904-4913, herein, "Krajcsi"). Claim 22 is summarized above. Claims 23 and 24 are drawn to limitations of the adenoviral vector of claim 22 wherein the retained E3 sequences that encode a functional 14.5K and 10.4K protein are the only E3 sequences remaining from the E3 region. More specifically, the 14.5K and 10.4K proteins form a RID complex. The teachings of Bout are summarized above. Bout recognizes the importance of the 14.7K protein and the RID complex, but is silent on the exclusive retention of E3 sequences that encode a functional 14.5K and 10.4K protein.

However, Krajcsi teaches that the E3 RID complex and the E3 14.7K protein independently act to inhibit tumor necrosis factor-induced apoptosis and TNF-induced release of arachidonic acid (abstract). It would have been obvious to retain only the sequences that encode the functional 14.5K and 10.4K proteins in Bout's vector. One would have been motivated to retain only those two proteins because they are a complex that work as a unit (RID complex) and

because they exhibit anti-inflammatory/apoptotic activity, evidenced by both Krajcsi (Krajcsi, abstract) and Bout (Bout, page 3, lines 11-12). One would have had a reasonable expectation of success that the RID complex would have been sufficient to reduce a host cell response against infected cells because Krajcsi discloses that the RID complex and the E3 14.7K protein act independently of each other. Therefore, the instant claims would have been obvious to one of ordinary skill in the art at the time the invention was made.

7. Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bout as applied to claim 22 above, and further in view of Kovesdi *et al.* (U.S. Patent 5,851,806, herein, "Kovesdi"). Claim 31 is drawn to a vector of claim 22 (summarized above), wherein the adenoviral vector of claim 22 has its E1 region deleted-in-part of rendered non-functional, and additionally, one of E2, E4 and L1-L5 are deleted or rendered non-functional. The teachings of Bout are summarized above. Bout discloses an adenoviral vector having an E1 deletion and portions of E3. Bout is silent on the additional deletion of at least one of E2, E4 and L1-L5.

However, Kovesdi discloses recombinant adenoviral vectors that have multiple region deletions (combinations of E1, E2A, E4 and E3 deletions). Kovesdi teaches that the deletion of these regions allows more space in the vector for large heterologous genes (col. 7, lines 27-35). It would have been obvious to delete more regions from Bout's adenoviral vector, as taught by Kovesdi. One would have been motivated by Kovesdi's teaching that the deletion of multiple regions from the vector creates more space for larger gene inserts. One would have had a reasonable expectation of success that the deletion of more regions from Bout's adenoviral vector would have worked to produce a viral particle (with larger heterologous genes) because

Kovesdi's adenoviral vector with multiple region deletions results in a viral particle expressing the desired gene inserts in gene therapy applications (Kovesdi, claims 47-61). Therefore, the instant claims would have been obvious to one of ordinary skill in the art at the time the invention was made.

8. Claims 32 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bout as applied to claim 22 above, and further in view of Kaplan *et al.* (U.S. Patent 6,100,086, herein, "Kaplan") and Kovesdi. Claims 32-33 are drawn to a vector of claim 22, wherein all or part of the E1 region and all of the native E3 region are deleted or rendered non-functional, and wherein the adenoviral vector portion is a modified adenovirus genome of a human adenovirus 5 (Ad5) and the retained sequence of E3 (RID complex) are isolated from the genome of the human adenovirus 2 (Ad2).

The teachings of Bout are summarized above. Bout's disclosure not only indicates that the retention of E3 sequence can be accomplished by deleting portions of E3 and retaining those that are desired, but the working example demonstrates the entire E1 and E3 region are deleted and replaced by Ad5 E3 in its entirety. Given Bout's teachings about retaining only those E3 sequences that encode protein that contribute to reduced inflammation/reduced host cell response to infected cells, one would have been motivated to incorporate only those particular sequences such as those that encode the RID complex. Bout teaches that the adenovirus vector is derived from adenovirus type 5 or adenovirus type 2 (Bout, page 20, claim 8.) Bout is silent on the combining of adenovirus types 5 and 2, and the further deletion/rendering non-function at least one of E2, E4, and L1-L5 regions.

However, Kaplan discloses recombinant adenoviral vectors that are chimeric, having combinations of adenoviral DNA from different serotypes such as Ad5 and Ad2 (Kaplan, col. 9, lines 38-48). It would have been obvious to produce a chimeric vector from Ad5 and Ad2. One would have been motivated to use the Ad5 vector genome and the Ad2 E3 sequences because diversity aids in avoiding the immune system. It is well known in the art that humans have pre-existing immunity to adenoviruses, making it challenging to evade the immune system. Diversity through chimeric constructions of vectors (Ad5 and Ad2) would have been a motivating factor in the field of adenovirus and gene therapy (Kaplan, col. 9, lines 49-63). One would have had a reasonable expectation of success that Ad2 E3 sequences would successfully be incorporated into an Ad5 vector, because Ad5 and Ad2 are well known in the art and preferred serotypes for gene therapy applications, as evidenced by Kaplan (Kaplan, col. 9, lines 42-43).

Further, Kovesdi discloses recombinant adenoviral vectors that have multiple region deletions (combinations of E1, E2A, E4 and E3 deletions). Kovesdi teaches that the deletion of these regions allows more space in the vector for large heterologous genes (col. 7, lines 27-35). It would have been obvious to delete more regions from Bout's adenoviral vector, as taught by Kovesdi. One would have been motivated by Kovesdi's teaching that the deletion of multiple regions from the vector creates more space for larger gene inserts. One would have had a reasonable expectation of success that the deletion of more regions from Bout's adenoviral vector would have worked to produce a viral particle (with larger heterologous genes) because Kovesdi's adenoviral vector with multiple region deletions results in a viral particle expressing the desired gene inserts in gene therapy applications (Kovesdi, claims 47-61). Therefore, the

instant claims would have been obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

9. No claim is allowed. Claim 25 is objected to. Claims 22-25 and 27-33 are rejected.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Stacy B. Chen
October 8, 2004